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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/660,131	09/11/2003	David H. Munn	M0351-287806	6907

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EXAMINER	
DEBERRY, REGINA M	

ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/660,131	MUNN ET AL.	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-48* is/are pending in the application.

4a) Of the above claim(s) *9,11,12,15 and 21-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10,13,14,16-20,47 and 48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Status of Application, Amendments and/or Claims

The amendment filed 21 December 2006 has been entered in full. Claims 1, 3-8, 10, 13, 14, 16-20, 47 and 48 are under examination.

The specification is in compliance with 37 CFR 1.821-1.825 of the Sequence Rules and Regulations.

The David Munn Declaration under 37 CFR 1.132 filed 21 December 2006 has been entered.

Information Disclosure Statement

The information disclosure statement(s)(IDS) filed 21 December 2006 was received and complies with the provisions of 37 CFR §§1.97 and 1.98. It has been placed in the application file and the information referred to therein has been considered as to the merits.

Withdrawn Objections And/Or Rejections

The rejection to claims 1, 3-8, 10, 13, 14, 16-20, 47 and 48 under 35 U.S.C. 112, first paragraph, enablement, as set forth at pages 4-9 of the previous Office Action (31 August 2006), is *withdrawn* in view of Applicant's arguments, submitted references and the David Munn Declaration under 37 CFR 1.132 (21 December 2006).

The rejection to claims 5 and 8 under 35 U.S.C. 112, second paragraph, as set forth at page 9 of the previous Office Action (31 August 2006), is *withdrawn* in view of the amendment and Applicant's arguments (21 December 2006).

NEW CLAIM REJECTIONS/OBJECTIONS

Claim Rejections-35 USC § 112, First Paragraph, Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-8, 13, 14, 16-20, 47, 48 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

A method to reduce recruitment of antigen presenting cells (APCs) (or their precursors or IDO+ dendritic cells) that inhibit T-cell proliferation to a tumor site (or tumor draining lymph node) in an individual, **wherein said APCs (or said precursors or said IDO+dentritic cells) express elevated levels of idoleamine 2,3-dioxygenase (IDO) and chemokine receptor CCR6 and wherein tumor site (or tumor draining lymph node) expresses MIP-3α**, comprising administering **a composition comprising an antibody to CCR6** to the subject to reduce recruitment of said APCs or (said precursors or said IDO+ dentritic cells),

does not reasonably provide enablement for the claims as currently claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The Munn declaration states that the *in vitro* assay used to measure MIP-3a is an assay that is well-accepted by those in the field of chemokine research as a method to measure the specificity and efficacy of chemokine-induced migration and/or the

inhibition of such chemokine-induced migration. The Munn declaration states that it is accepted practice in the field of chemokine research to use this type of chemotaxis assay to predict chemokine-induced migration of dentritic cells that can occur *in vivo*. The Munn declaration states that the data in the specification confirms that the *in vitro* model used to measure chemotaxis of IDO+ APCs towards a MIP-3a gradient accurately predicts the biological relevant properties of the IDO+ cells found *in vivo*. The Munn declaration states that the specification shows that at least some tumors and tumor-draining lymph nodes express MIP-3a and that IDO+ APCs are found in such MIP-3a expressing tumors and/or tumor-draining lymph nodes. The Munn declaration states that subsequent work has shown that immunosuppressive, tolerance-inducing DCs isolated from the tumor-draining lymph nodes of mice preferentially express CCR6 and CD123. In contrast, non-suppressive IDO-negative DCs from the same nodes express much lower levels of CCR6 and CD123. The Munn declaration states that when murine IDO+ CCR6+DCs were injected into new, tumor free mice, it was found that these cells were able to create an antigen-specific anergy in the host T cells. Development of such antigen-specific anergy was prevented by the administration of IDO inhibitor, 1-MIT.

The Munn Declaration under 37 CFR 1.132 filed 21 December 2006 is sufficient to overcome the rejection of claims 1, 3-8, 10, 13, 14, 16-20, 47 and 48 based upon 35 USC 112, first paragraph, enablement. However, this is not tantamount to the scope of the claims as currently recited. The instant specification teaches that once established, human tumors are not rejected by the immune system, a state of functional tolerance

occurs, which eventually proves fatal to the host. The specification teaches that tolerance inducing APC express elevated levels of idoleamine 2,3-dioxygenase (IDO) and chemokine receptor CCR6. MIP-3a is the known ligand for CCR6. The specification teaches that certain tumors express the chemotaxis factor MIP-3a (page 8, lines 27-30 and page 9, lines 23-27). The specification teaches abnormal infiltration of IDO+ cells in samples of tumor and tumor-draining lymph nodes from patients with malignant melanoma (pages 48-50). The specification teaches MIP-3a expression in malignant melanoma (pages 51, lines 3-12). MIP-3a induced chemotaxis of CCR6+APCs is blocked by CCR6 antibody (page 53). The purported utility is administering CCR6 antibodies to block the signal between IDO+ APC and tumors expressing MIP-3a (to reduce recruitment of IDO+ APC).

The claims fails to bear a reasonable correlation with the scope of enabling disclosure set forth in the specification because the instant specification fails to teach a method of reducing IDO+ APCs to any particular site in a subject or wherein the subject has any type of tumor or tumor draining lymph node (versus a **tumor or tumor draining lymph node that expresses MIP-3α)**. The instant specification fails to demonstrate a method of reducing IDO+APCs **that does not express chemokine receptor CCR6.** Lastly, the specification fails to demonstrate that any composition can be administered to a subject to reduce IDO+ APCs **(versus a composition comprising an antibody to CCR6).** The specification states that it would be desirable to prevent the migration of tolerogenic APC to sites such as tumors, where they are detrimental, while still allowing migration of non-tolerogenic APC to those sites (page 2, line 28-page 3,

line 2). Thus, CCR6 must be expressed on IDO+ APC to selectively inhibit recruitment, but allow immuno-recognition by the CCR6 antibody. In addition, the tumor or tumor draining lymph node must express MIP-3a (sole ligand of CCR6) to **preferentially recruit IDO+ APC CCR6+ expressing cells**.

Due to the inherent unpredictability in the field and the lack of guidance in the specification regarding a method to reduce recruitment of IDO+APCs (precursors or IDO+ dentritic cells) that do not express chemokine receptor CCR6 comprising administering any composition to a tumor (or tumor draining lymph node) that does not express MIP-3a in a subject, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, and the breadth of the claims which fail to recite limitations regarding the types of APCs and tumors that can be modulated and compositions that can be administered to a subject, one of skill in the art would be forced into undue experimentation without a reasonable expectation of success in order to practice the claimed invention in its full scope.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3-8, 10, 13, 14, 16-20, 47 and 48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claims are indefinite because of the interchangeable use of "IDO+ APCs"(claims 1 and 16) and "IDO+ antigen presenting cells (APCs)(claims 4, 6 and 18). It is unclear the difference between the instant claims and thus the metes and bounds cannot be determined.

Claims 1 and 16 are indefinite in its recitation, "a method to reduce recruitment of **antigen presenting cells (APCs)**...comprising administering a composition to the subject to reduce recruitment of **IDO+ APCs or their precursors**..." The breadth of the instant claim is not clear because the preamble (antigen presenting cells (APCs)) and the body of the claim (IDO+ APCs or their precursors) are not consistent.

Claim 16 is indefinite in its recitation, "a method to reduce recruitment of antigen presenting cells (APCs) that inhibit T-cell proliferation **to a tumor in a subject**...comprising administering a composition to the subject to reduce recruitment of IDO+ APCs or their precursors **to at least one of a tumor or a tumor draining lymph node in a subject**..." The breadth of the instant claim is not clear because the preamble (a tumor) and the body of the claim (at least one of a tumor or a tumor draining lymph node in a subject) are not consistent.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

RMD
4/30/07

Marianne P. Allen

MARIANNE P. ALLEN
PRIMARY EXAMINER

5/3/07

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